

WHAT IS CLAIMED IS:

1. A ~~human keratinocyte growth factor (KGF) having an apparent molecular weight of about 28 kDa as determined by migration in NaDODSO₄/PAGE, and a specific activity of at least about 3.4 x 10⁴ units per milligram of protein, where one unit of activity is defined as that amount which causes half of the maximal possible stimulation of DNA synthesis in BALB/MK keratinocyte cells under standard assay conditions.~~
2. Human KGF according to claim 1, wherein said specific activity is at least about 3.2 x 10⁵ units per milligram protein.
3. A bioassay for KGF-like activity in a test sample which comprises the following steps:
 - i) growing keratinocytes in culture to confluence and maintaining said confluent culture in serum-free medium;
 - ii) adding a test sample to said confluent culture of keratinocytes; and
 - iii) determining the stimulation of DNA synthesis in said keratinocytes.

4. A method of producing KGF from
cultured cells comprising the following steps:

- i) Culturing KGF-producing cells in
culture medium under conditions
such that KGF is produced;
- 5 ii) concentrating said culture medium
so that a first concentrate is
formed;
- 10 iii) contacting said concentrate with
heparin under conditions such that
KGF present in said first
concentrate binds to the heparin
whereby a heparin-KGF complex is
formed;
- 15 iv) separating said heparin-KGF complex
from said concentrate;
- v) treating said heparin-KGF complex
under conditions such that said KGF
dissociates from the heparin so
that a solution of free KGF is
formed;
- 20 vi) concentrating said solution so that
a second concentrate is formed;
- vii) fractionating said second
concentrate so that KGF is
separated from the remaining
components.

5. A method of producing KGF from cultured cells, according to claim 4, wherein said KGF-producing cells are M426 human embryonic fibroblasts.

5 6. A DNA segment encoding a human keratinocyte growth factor (KGF) protein.

7. A DNA segment, according to claim 6, wherein said protein has the amino acid sequence defined in Figure II-1.

10 8. A DNA segment encoding a chimeric KGF-like protein which comprises within a single polypeptide molecule functional segments of human KGF and at least one other polypeptide of the fibroblast growth factor family.

15 9. A recombinant DNA molecule comprising a DNA segment according to claim 6 or claim 8 and a vector.

10. A culture of cells transformed with said recombinant DNA molecule according to claim 9.

20 11. A method of producing a human KGF protein comprising culturing said cells according to claim 10 in a culture medium under conditions such that said protein is produced and isolating said protein from said cells.

25 12. A method of producing a human KGF protein comprising culturing said cells according to claim 10 in a culture medium, wherein said

protein is secreted from said cell, and isolating said protein from said medium.

13. A human KGF or KGF-like protein having the amino acid sequence in Figure II-1B.

5 14. A human KGF or KGF-like protein, according to claim 13, which is not glycosylated.

15. An antibody specific for a peptide having the amino acid sequence of human KGF or KGF-like protein, according to claim 13.

10 16. The antibody according to claim 15 which neutralizes the mitogenic activity of human KGF.

17. A bioassay for expression of a gene encoding KGF, comprising the steps of:

15 i) isolating mRNA from tissues or cells;

and

ii) annealing said RNA to a DNA probe encoding a human KGF;

20 iii) determining the amount of DNA:RNA hybrid containing said DNA probe.

18. A bioassay for KGF antigen comprising the steps of:

i) extracting polypeptides from body fluids or tissue samples;

5 and

ii) determining the level of human KGF antigen by reaction with an antibody specific for a peptide having the amino acid sequence of human KGF or KGF like protein, according to claim 13.

10 19. A pharmaceutical composition for treatment of conditions requiring specific stimulation of epithelial cells, comprising KGF according to claim 1 or claim 13, and an acceptable pharmaceutical carrier.

15 20. A pharmaceutical composition for treatment of conditions requiring specific inhibition of stimulation of epithelial cells by KGF, comprising antibodies to KGF according to claim 15, and an acceptable pharmaceutical carrier.

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B'7

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F-34

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N5